REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The claims have been revised to define the invention with additional clarity. That the claims have been amended should not construed that Applicants agreed with any position taken by the Examiner. Rather, the revisions are offered merely to advance prosecution and Applicants reserve the right to pursue any deleted subject matter in a continuing application.

The claims as presented are fully supported by an enabling disclosure. As regards the revision of claims 28 and 62, the Examiner's attention is directed to page 23 where support for the disorders and target molecule of (i) can be found, to page 19 where support for the disorders and target molecules of (ii) can be found, to pages 18 and 19 where support for the disorder and target molecules of (iii) can be found, to page 20 where support for the disorder and target molecule of (iv) can be found, to page 22 where support for the disorder and target molecule of (iv) can be found, to page 22 where support for the disorder and target molecule of (v) can be found, to page 17 where support for the disorder and target molecules of (vi) can be found, to page 20 where support for the disorder and target molecule of (vii) can be found, to page 22, where support for the disorder and target molecules of (viii) can be found, and to page 23 where support for the disorder and target molecules of (ix) can be found.

Claims 28, 29, 33, 40, 42, 49, 50, 52-54, 57, 62 and 63 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim revisions and further in view of the comments that follow.

In rejecting the claims as non-enabled, the Examiner contends that there is a lack of guidance in the specification as regards the binding specificity of the recited binding molecule. While not agreeing with the Examiner, the above-noted claim revisions are believed to address any concern that the Examiner might have.

As the Examiner is aware, the focus of present invention is not on novel binding specificities (i.e., the variable region of antibodies) but rather is on novel effector domains (i.e., the constant region of antibodies). The effector domains of the invention can be freely combined with conventional binding domains for use in the claimed methods. Only those binding molecules incorporating the effector domains of the present invention are encompassed by the claims.

As to whether there is a reasonable correlation between of the disclosure and the scope of the claims, Applicants submit that there is. The Examiner's assertion to the contrary, the claims do not require that a binding molecule of the invention have the capacity to treat "all diseases". The claims as presented recite the diseases/disorders and relevant target molecules for which the binding molecule has binding specificity.

The combinations of disease/disorders and target molecule are all known in the art. For example, the disorders recited in the first clause of claim 28 (graft-vs-host disease or host-vs-graft disease, organ transplant rejection, bone-marrow transplant rejection, autoimmune vasculitis, arthritis and asthma) include a T-cell mediated element. It may, therefore, be desirable to treat them with an antibody that blocks T-cell function, for example, through targeting and blocking of the T-cell receptor complex. It is known that part of the T-cell receptor complex is the co-receptor molecule known as CD3. Non-depleting blocking antibodies to CD3 (including OKT3 discussed on page 23 of the application) have been shown to be successful in

immunosuppression of such auto- and allo-immune diseases. (This can be shown by simply typing "OKT3" into an internet search engine.)

As to providing the antibodies, suitable variable regions have also been described in the literature for the specificities recited in claim 28. This was the case for the Fog-1 variable region DNAs of Example 1. In any case, and as previously submitted, given an appropriate target molecule, DNA encoding antibody variable regions with a desired binding specificity can be obtained by several methods, including reverse transcription and PCR from many sources, including antibody-secreting cell lines or the B-cells of an individual. This is well within the ambit of the skilled person.

Indeed, the court concluded, in *In re Wands* (cited by the Examiner), that:

> "...it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." Id., 8 USPQ2d at 1407.

Applicants submit the same conclusion should apply here.

As regards the Examiner's comments relating to the absence of *in* vivo data, Applicants offer the following.

The presence of working *in vivo* examples is **not** required by the statute, rules, or the case law. Indeed, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985), all that is required is that:

> "...based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence."

As noted in previous responses, the presently claimed molecules have been tested for numerous effector functions as described in Figures 1 to 14 and Examples 1 to 6b. Furthermore, they have

been shown to inhibit the response of monocytes to immunoglobulins sensitized cells and inhibit the killing of targeted cells through complement lysis or ADCC. As discussed in the Examples (e.g., page 49, lines 30-34), the tests used have been those already shown to be useful in predicting *in vivo* pathology. The tests on page 50 studied CL responses which were indicative of haemolytic disease in the newborn. In addition, the Examiner's attention is drawn to Appendix III of the response filed December 30, 2004, which includes a discussion of a human volunteer study.

Therefore, it is submitted it would be reasonable to expect activity *in vivo* of the presently claimed immunoglobulins in the specified indications characterized by the specified target molecules.

With reference to the Examiner's comments at the top of page 5 of the Action, Applicants do not agree with the Examiner's position as regards claim 33 and 42. Nonetheless, these claims have been revised to read "consist of".

Claims 50, 52 and 53 relate to nucleic acids comprising specified sequences. The Examiner offers no well founded reason as to why an encoding-nucleotide sequence would not be expected to serve the intended function (i.e., expression of a polypeptide) simply because it includes additional nucleotides at its termini. Indeed, the opposite is true. Most coding sequences occur and are utilized only in the context of longer nucleic acids, i.e., genomes or recombinant constructs.

Additionally, the attention of the Examiner is drawn to "TRAINING MATERIALS FOR EXAMINING PATENT APPLICATIONS WITH RESPECT TO 35 U.S.C. SECTION 112, FIRST PARAGRAPH-ENABLEMENT CHEMICAL/BIOTECHNICAL APPLICATIONS", and specifically "Example N: DNA".

In that case the claim referred to:

"An isolated cDNA that ***comprises*** the following DNA sequence...[recited sequences]... or fragments thereof that are at least 15 nucleotides in length. (emphasis added)
The conclusion is that:

"Claim 1 is limited to a single DNA sequence and any 15 mer thereof. Since the state of the art is such that it would have been routine to make the DNA given the sequence, it certainly would not require undue experimentation to make the DNAs claimed in claim 1."

This conclusion would seem to be contradictory to the Examiner's position that the word "comprising" in such contexts gives rise to undue experimentation.

Finally, the Examiner's suggested revision of claims 40 and 49 has been adopted.

Reconsideration is requested.

Claims 57 and 62 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. The rejection is traversed.

Claim 57 (and likewise claim 28) has been revised in a manner which is believed to address the Examiner's concerns. The objection to claims 58 to 61 is therefore moot.

The Examiner contends that the dependency of claim 62 on claim 58 is ambiguous. Claim 58 (and claim 24) has been revised to improve clarity – it is apparent from the teachings of the specification that it is the effector domain that binds the FcγRIIb receptor to achieve the specified inhibition – see specification pages 12, line 18 – page 13, line 28. The binding domain is capable of binding a target molecule relevant to the disease, as specified in claim 62.

In view of the above, reconsideration is requested.

ARMOUR et al.
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This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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